

CLAIMS

1. A method for preparing a delivery composition comprising admixing a first lipid comprising 1,2-diacyl-sn-glycero-3-ethylphosphocholine, a second lipid, and two or more cationic polymers, wherein the admixing produces a composition for delivering a selected molecule to a cell.
2. The method of claim 1, wherein the second lipid is a polymer-linked lipid.
3. The method of claim 2, wherein the polymer-linked lipid is 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-5000].
4. The method of claim 2, wherein the polymer-linked lipid is 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000].
5. The method of claim 1, wherein the cationic polymers are polyethyleneimine and protamine.
6. The method of claim 5, wherein the ratio of polyethyleneimine to protamine is between about 0.01:1 and about 0.2:1.
7. The method of claim 5, wherein the ratio of polyethyleneimine to protamine is about 0.02:1.
8. The method of claim 1, wherein the cationic polymers are polylysine and protamine.
9. The method of claim 8, wherein the ratio of polylysine to protamine is between about 0.1:1 and about 1:1.
10. The method of claim 8, wherein the ratio of polylysine to protamine is about 0.3 to 1.
11. The method of claim 1, wherein the cationic polymers are polyethyleneimine, protamine and polylysine.
12. The method of claim 11, wherein the ratio of polyethyleneimine to protamine to polylysine is between about 0.002:0.05:1 and about 0.02:0.5:1.
13. The method of claim 11, wherein the ratio of polyethyleneimine to protamine to polylysine is about 0.01:0.3:1.

14. The method of claim 1, wherein the ratio of the cationic polymer and the selected molecule is between about 2:0.1 and about 10:5.
15. The method of claim 1, wherein the ratio of the second lipid and the selected molecule is between about 0.2:0.1 and about 5:5.
- 5 16. The method of claim 1, wherein the ratio of 1,2-diacyl-sn-glycero-3-ethylphosphocholine and the selected molecule is between about 0.2:0.1 and about 10:5.
17. The method of claim 1, wherein the selected molecule is a DNA.
18. The method of claim 1, wherein the selected molecule is a oligonucleotide.
19. The method of claim 1, wherein the selected molecule is a RNA.
- 10 20. The method of claim 1, wherein the selected molecule is a protein.
21. The method of claim 1, wherein the selected molecule is a drug.
22. The method of claim 21, wherein the drug is a chemotherapeutic agent.
23. The method of claim 1, wherein the selected molecule is an expression construct.
- 15 24. The method of claim 23, wherein the expression construct expresses a biologically functional protein or peptide.
25. The method of claim 24, wherein the biologically function protein or peptide is a tumor suppressor, a tumor suppressor activator, a pro-apoptotic factor, an oncogenic blocker, or an anti-angiogenesis factor.
26. The method of claim 25, wherein the tumor suppressor is p53.
- 20 27. The method of claim 1, wherein the cell is a cancer cell or a macrophage cell.
- 25 28. The method of claim 27, wherein the cancer cell is metastatic lung cancer cell, a head and neck cancer cell, a thyroid cancer cell, a liver cancer cell, a breast cancer cell, a prostate cancer cell, a ovarian cancer cell, a colon cancer cell, a rectum cancer cell, a pancreas cancer cell, a spleen cancer cell, a stomach cancer cell, a duodenum cancer cell, a kidney cancer cell, a uterus cancer cell, a cervical cancer cell, a testicle cancer cell, a brain

cancer cell, a bone cancer cell, a lymphoid cancer cell, a skin cancer cell, or a vesicular cancer cell.

29. The method of claim 27, wherein the cancer cell is a metastatic lung cancer cell.

30. The method of claim 29, wherein the metastatic lung cancer cell is a small cell lung carcinoma cell.

31. A method for delivering a selected molecule to a cell comprising:

(a) providing a composition comprising:

(i) a first lipid comprising 1,2-diacyl-sn-glycero-3-ethylphosphocholine;

(ii) a second lipid;

(iii) two or more cationic polymers;

(iv) the selected molecule, and

(b) contacting said cell with said composition.

32. The method of claim 31, wherein the second lipid is a polymer-linked lipid.

33. The method of claim 32, wherein the polymer-linked lipid is 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-5000].

34. The method of claim 32, wherein the polymer linked lipid is 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000].

35. The method of claim 31, wherein the cationic polymers are polyethyleneimine and protamine.

36. The method of claim 35, wherein the ratio of polyethyleneimine to protamine is between about 0.01:1 and about 0.2:1.

37. The method of claim 35, wherein the ratio of polyethyleneimine to protamine is about 0.02:1.

38. The method of claim 31, wherein the cationic polymers are polylysine and protamine.

39. The method of claim 38, wherein the ratio of polylysine to protamine is between about 0.1:1 and about 1:1.

40. The method of claim 38, wherein the ratio of polylysine to protamine is about 0.3 to 1.

41. The method of claim 31, wherein the cationic polymers are polyethyleneimine, protamine and polylysine.
42. The method of claim 41, wherein the ratio of polyethyleneimine to protamine to polylysine is between about 0.002:0.05:1 and about 0.02:0.5:1.
- 5 43. The method of claim 41, wherein the ratio of polyethyleneimine to protamine to polylysine is about 0.01:0.3:1.
44. The method of claim 31, wherein the ratio of the cationic polymer and the selected molecule is between about 2:0.1 and about 10:5.
- 10 45. The method of claim 31, wherein the ratio of the second lipid and the selected molecule is between about 0.2:0.1 and about 5:5.
46. The method of claim 31, wherein the ratio of 1,2-diacyl-sn-glycero-3-ethylphosphocholine and the selected molecule is between about 0.2:0.1 and about 10:5.
47. The method of claim 31, wherein the selected molecule is a DNA.
48. The method of claim 31, wherein the selected molecule is a oligonucleotide.
- 15 49. The method of claim 31, wherein the selected molecule is a RNA.
50. The method of claim 31, wherein the selected molecule is a protein.
51. The method of claim 31, wherein the selected molecule is a drug.
52. The method of claim 51, wherein the drug is a chemotherapeutic agent.
53. The method of claim 31, wherein the selected molecule is an expression construct.
- 20 54. The method of claim 53, wherein the expression construct expresses a biologically functional protein or peptide.
55. The method of claim 54, wherein the biologically function protein or peptide is a tumor suppressor, a tumor suppressor activator, a pro-apoptotic factor, an oncogenic blocker, or an anti-angiogenesis factor.
- 25 56. The method of claim 54, wherein the tumor suppressor is p53.

57. The method of claim 31, wherein the cell is a cancer cell or a macrophage cell.
58. The method of claim 57, wherein the cancer cell is a metastatic lung cancer cell, a head and neck cancer cell, a thyroid cancer cell, a liver cancer cell, a breast cancer cell, a prostate cancer cell, a ovarian cancer cell, a colon cancer cell, a rectum cancer cell, a pancreas cancer cell, a spleen cancer cell, a stomach cancer cell, a duodenum cancer cell, a kidney cancer cell, a uterus cancer cell, a cervical cancer cell, a testicle cancer cell, a brain cancer cell, a bone cancer cell, a lymphoid cancer cell, a skin cancer cell, or a vesicular cancer cell.
59. The method of claim 57, wherein the cancer cell is a metastatic lung cancer cell.
60. The method of claim 59, wherein the metastatic lung cancer cell is a small cell lung carcinoma cell.
61. The method of claim 31, wherein the cell is in a subject.
62. The method of claim 61, wherein the subject is a mammal.
63. The method of claim 62, wherein the mammal is a human.
64. A method for treating cancer comprising administering to a subject a composition comprising:
- a) a first lipid comprising 1,2-diacyl-sn-glycero-3-ethylphosphocholine;
 - b) a second lipid;
 - c) two or more cationic polymers; and
 - d) a therapeutically effective amount of an anticancer agent.
65. The method of claim 64, wherein the cancer is a primary or metastatic cancer.
66. The method of claim 65, wherein the primary or metastatic cancer is a lung cancer, a head and neck cancer, a thyroid cancer, a liver cancer, a breast cancer, a prostate cancer, a ovarian cancer, a colon cancer, a rectum cancer, a pancreas cancer, a spleen cancer, a stomach cancer, a duodenum cancer, a kidney cancer, a uterus cancer, a cervical cancer, a testicle cancer, a brain cancer, a bone cancer, a lymphoid cancer, a skin cancer, or a vesicular cancer.
67. The method of claim 65, wherein the cancer is a metastatic lung cancer.

68. The method of claim 67, wherein the metastatic lung cancer is a small cell lung carcinoma.
69. The method of claim 64, wherein the subject is a mammal.
70. The method of claim 69, wherein the mammal is a human.
- 5 71. The method of claim 64, wherein administering is intravenously, intraperitoneally, intratracheally, or by inhalation.
72. The method of claim 71, wherein administering may be once.
73. The method of claim 71, wherein administering may be more than once.
74. The method of claim 64, wherein the second lipid is a polymer-linked lipid.
- 10 75. The method of claim 74, wherein the polymer-linked lipid is 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-5000].
76. The method of claim 74, wherein the polymer-linked lipid is 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000].
- 15 77. The method of claim 64, wherein the cationic polymers are polyethyleneimine and protamine.
78. The method of claim 77, wherein the ratio of polyethyleneimine to protamine is between about 0.01:1 and about 0.2:1.
79. The method of claim 77, wherein the ratio of polyethyleneimine to protamine is about 0.02:1.
- 20 80. The method of claim 64, wherein the cationic polymers are polylysine and protamine.
81. The method of claim 80, wherein the ratio of polylysine to protamine is between about 0.1:1 and about 1:1.
82. The method of claim 80, wherein the ratio of polylysine to protamine is about 0.3 to 1.
- 25 83. The method of claim 64, wherein the cationic polymers are polyethyleneimine, protamine and polylysine.

84. The method of claim 83, wherein the ratio of polyethyleneimine to protamine to polylysine is between about 0.002:0.05:1 and about 0.02:0.5:1.
85. The method of claim 83, wherein the ratio of polyethyleneimine to protamine to polylysine is about 0.01:0.3:1.
- 5 86. The method of claim 64, wherein the ratio of the cationic polymer and the anticancer agent is between about 2:0.1 and about 10:5.
87. The method of claim 64, wherein the ratio of the second lipid and the anticancer agent is between about 0.2:0.1 and about 5:5.
- 10 88. The method of claim 64, wherein the ratio of 1,2-diacyl-sn-glycero-3-ethylphosphocholine and the anticancer agent is between about 0.2:0.1 and about 10:5.
89. The method of claim 64, wherein the anticancer agent is a DNA.
90. The method of claim 64, wherein the anticancer agent is a oligonucleotide.
91. The method of claim 64, wherein the anticancer agent is a RNA.
92. The method of claim 64, wherein the anticancer agent is a protein.
- 15 93. The method of claim 64, wherein the anticancer agent is a drug.
94. The method of claim 93, wherein the drug is a chemotherapeutic agent.
95. The method of claim 64, wherein the anticancer agent is an expression construct.
96. The method of claim 95, wherein the expression construct expresses a biologically functional protein or peptide.
- 20 97. The method of claim 96, wherein the biologically functional protein or peptide is a tumor suppressor gene, a tumor suppressor activator, a pro-apoptotic factor, an oncogenic blocker or an anti-angiogenesis factor.
98. The method of claim 97, wherein the tumor suppressor gene is p53.
99. A composition comprising:
- 25 a) a first lipid comprising 1,2-diacyl-sn-glycero-3-ethylphosphocholine;

- b) a second lipid; and
- c) two or more cationic polymers.

100. The composition of claim 99, wherein the second lipid is a polymer-linked lipid.

5 101. The composition of claim 100, wherein the polymer-linked lipid is 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-5000].

102. The composition of claim 100, wherein the polymer-linked lipid is 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000].

103. The composition of claim 99, wherein the cationic polymers are polyethyleneimine and protamine.

10 104. The composition of claim 103, wherein the ratio of polyethyleneimine to protamine is between about 0.01:1 and about 0.2:1.

105. The composition of claim 103, wherein the ratio of polyethyleneimine to protamine is about 0.02:1.

15 106. The composition of claim 99, wherein the cationic polymers are polylysine and protamine.

107. The composition of claim 106, wherein the ratio of polylysine to protamine is between about 0.1:1 and about 1:1.

108. The composition of claim 106, wherein the ratio of polylysine to protamine is about 0.3 to 1.

20 109. The composition of claim 99, wherein the cationic polymers are polyethyleneimine, protamine and polylysine.

110. The composition of claim 109, wherein the ratio of polyethyleneimine to protamine to polylysine is between about 0.002:0.05:1 and about 0.02:0.5:1.

25 111. The composition of claim 109, wherein the molar ratio of polyethyleneimine to protamine to polylysine is about 0.01:0.3:1.

112. The composition of claim 99, further comprising an agent.

113. The composition of claim 112, wherein the ratio of the cationic polymer and the agent is between about 2:0.1 and about 10:5.
114. The composition of claim 112, wherein the ratio of the second lipid and the agent is between about 0.2:0.1 and about 5:5.
- 5 115. The composition of claim 112, wherein the ratio of 1,2-diacyl-sn-glycero-3-ethylphosphocholine and the agent is between about 0.2:0.1 and about 10:5.
116. The composition of claim 112, wherein the agent is a DNA.
117. The composition of claim 112, wherein the agent is a oligonucleotide.
118. The composition of claim 112, wherein the agent is a RNA.
- 10 119. The composition of claim 112, wherein the agent is a protein.
120. The composition of claim 112, wherein the agent is a drug.
121. The method of claim 120, wherein the drug is a chemotherapeutic agent.
122. The composition of claim 112, wherein the agent is an expression construct.
- 15 123. The method of claim 122, wherein the expression construct expresses a biologically functional protein or peptide.
124. The method of claim 123, wherein the biologically functional protein or peptide is a tumor suppressor gene, a tumor suppressor activator, a pro-apoptotic factor, an oncogenic blocker or an anti-angiogenesis factor.
125. The composition of claim 124, wherein the tumor suppressor gene is p53.